

**BEST AVAILABLE COPY**

**THE PATENTS ACT, 1970**

It is hereby certified that annexed hereto is a true copy of  
Application, Complete Specification, Abstract & Drawings of the  
extract of Patent Application No.523/CHE/2003, dated 26/06/2003 by  
M/s. Dr. Reddy's Laboratories Limited, having its registered office at  
7-1-27, Ameerpet, Hyderabad 500 016, Andhra Pradesh, India.

.....In witness thereof

I have hereunto set my hand

Dated this the 26<sup>th</sup> day of July 2004

*M. S. Venkataraman*

(M.S. VENKATARAMAN)

Assistant Controller of Patents & Designs

*[Signature]*

**CERTIFIED COPY OF  
PRIORITY DOCUMENT**

**PATENT OFFICE BRANCH  
GOVERNMENT OF INDIA**

**Government Complex, 6<sup>th</sup> Floor, Annex.II**

**No. 43, Anna Salai, Teynampet, Chennai – 600 018**

FORM 1

THE PATENTS ACT, 1970  
(39 of 1970)  
APPLICATION FOR GRANT OF A PATENT  
(Section 5(2), 7, 54 and 135 and Rule 33A)

1. I/We, Dr. Reddy's Laboratories Limited, an Indian company having its registered office at 7-1-27, Ameerpet, Hyderabad, Andhra Pradesh, INDIA, 500 016
2. hereby declare -
  - (a) that I am/ we are in possession of an invention titled "**Novel amorphous form of Dutasteride and process for preparation thereof**"
  - (b) that the complete specification relating to this invention is filed with this application.
  - (c) that there is no lawful ground of objection to the grant of a patent to us.
3. further declare that the inventor(s) for the said invention is/are **Manne Satyanarayana Reddy, Gudipati Srinivasulu, Mandava Venkata Naga Brahmeswararao, Bojja Rama chandra Reddy and Singamsetty Radhakrishna**. All citizens & residents of India belonging to **Dr. Reddy's Laboratories Limited, 7-1-27, Ameerpet, Hyderabad - 500 016, Andhra Pradesh**.
4. We claim the priority from the application(s) filed in convention countries, particulars of which are as follows.
5. We state that the said invention is an improvement in or modification of the invention, the particulars of which are as follows and of which I/We are the applicant/patantee
6. We state that the application is divided out of my/our application, the particulars of which are given below and pray that this application deemed to have been filed on \_\_\_\_\_ under section 16 of the Act.
7. That We are the assignee or legal representative of the true and first inventors.
8. That my/our address for service in India is as follows:

Dr. Manne Satyanarayana Reddy  
Vice-President-R&D  
Dr. Reddy's Laboratories Limited  
7-1-27, Ameerpet  
Hyderabad, A.P., 500 016  
Phone: 040- 3095578  
Fax: 040-3095438

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 5998   
 26.06.03   
 26/6

9. Following declaration was given by the inventor(s) or applicant(s) in the convention country:

We, the true and first inventors for this invention or the applicant(s) in the convention country declare that the applicant(s) herein is/are my/our assignee or legal representative

(Signed) M. S. Reddy  
Manne Satyanarayana Reddy,  
H.No. 8-3-167/D/16,  
Kalyan Nagar,  
Near AG Colony,  
Erragadda,  
Hyderabad-500 038.

(Signed) G. Venkatesh  
Gudipati Srinivasulu,  
15-21-107,  
Balajinagar,  
Kukatpally,  
Hyderabad – 500 072.

(Signed) B. Venkatesh  
Mandava Venkata Naga Brahmeswararao,  
Plot No:98,  
Vasantanagar colony,  
Kukatpally,  
Hyderabad – 500 072.

(Signed) B. Ramachandra Reddy  
Bojja Ramachandra Reddy,  
LIG-537,  
KPHB Colony,  
kukatpally,  
Hyderabad. - 500072


(Signed) S.R. Krishna  
Singamsetty Radhakrishna  
H.No:15-21-149/3  
Balajinagar  
Kukatpally  
Hyderabad-500072

10. That to the best of my/our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to me/us on this application.
11. Following are the attachments with the application
- (a) Complete specification (~~---2---~~<sup>2</sup> pages, in triplicate)
  - (b) Drawings (~~-----~~<sup>2</sup> pages, in triplicate)
  - (c) Priority documents(s)
  - (d) Statement and Undertaking on Form-3.
  - (e) Power of authority
  - (f) Abstract of the invention (~~-----~~<sup>1</sup> page, in triplicate)

I/We request that a patent may be granted to me/us for the said invention.

Dated this 23<sup>rd</sup> day of June 2003.

To,  
The Controller of Patents  
The Patents Office Branch, Chennai.

(Signed)   
Dr. Manne Satyanarayana Reddy,  
Vice-President (R&D)  
Dr. Reddy's Laboratories Limited.

**FORM 2**

**THE PATENTS ACT, 1970**

**COMPLETE SPECIFICATION**

**(SECTION 10)**

**Novel Amorphous form of Dutasteride and Process for  
preparation thereof.**

**Dr. Reddy's Laboratories Ltd.**

**an Indian Company having its registered office at**

**7-1-27, Ameerpet**

**Hyderabad – 500 016, A.P., India**

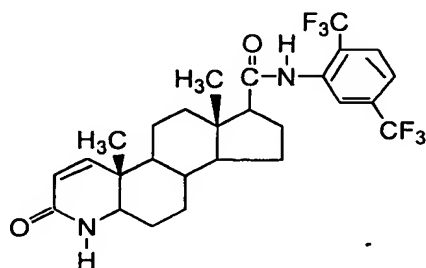
The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed:

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**Field of the Invention:**

The present invention relates to novel amorphous form of Dutasteride, which is chemically known as 17 $\beta$ -N-[2,5-bis (Trifluoromethyl) phenyl] carbamoyl-4-aza-5 $\alpha$ -androst-1-en-3-one and shown as Formula (I). The present invention relates to process for preparing the novel amorphous form of Dutasteride.



Formula (I)

Dutasteride is useful in the treatment of androgen responsive and mediated diseases.

**Background of the invention:**

US Patent 5,565,467 claimed Dutasteride and its related compounds. It also claimed the pharmaceutical formulations thereof and their use in the treatment of androgen and mediated diseases.

The '467 patent discloses a process for the preparation of Dutasteride, which comprises the dehydrogenation of 17 $\beta$ -N-(2,5-bis (Trifluoromethyl) phenyl) carbamoyl-4-aza-5 $\alpha$ -androstane-3-one in the presence of catalysts 2,3 -dichloro-5, 6-dicyano-1, 4-benzoquinone (DDQ) and bis (tri methylsilyl) trifluoroacetamide in dioxane as solvent and the resultant solid is crystallized from a mixture of ethyl acetate - heptane in a ratio of 1:1 v/v.

WO 9507927 disclosed the process for isolation of pure Dutasteride by crystallization of crude Dutasteride in Methanol and acetonitrile.

our provisional specification (application No: 534/MAS/2002) discloses the crystalline polymorphic forms designated as Form-I and Form-II and process for their preparation.

No relevant references of Dutasteride amorphous form were disclosed till date.

Polymorphism can be defined as the ability of the same chemical substance to exist in different crystalline structures. The different structures are referred to as polymorphs, polymorphic modification or form.

Hence, the first object of the present invention is to provide the novel amorphous form of Dutasteride.

The second object of the present invention is the process for the preparation of the novel amorphous form of Dutasteride.

The amorphous form of the present invention is characterized by X-ray diffractogram pattern.

The novel amorphous form of Dutasteride may be well suited for pharmaceutical formulations and can be used in the treatment of androgen and mediated diseases.

**Brief description of accompanying drawings:**

Fig-1: X-Ray powder diffractogram of Dutasteride amorphous.

Fig.-2: Infrared spectrum of Dutasteride amorphous

**Summary of the invention:**

The present invention provides novel amorphous form of Dutasteride and process for preparation thereof. The amorphous of Dutasteride are characterized by X-ray diffractogram pattern. The process for the preparation of the amorphous form comprises the dissolution of Dutasteride in polar organic solvents accompanied by distillation of the solvent to afford the novel amorphous form.

**Detailed description of the invention:**

The present invention provides the novel amorphous form of Dutasteride and process for its preparation.

The amorphous form of Dutasteride of present invention is characterized by X-ray diffractogram, which are measured on Bruker Axe, DS Advance Powder X-ray Diffractometer with Cu K alpha-1 Radiation source.

The process for the preparation of novel amorphous form of Dutasteride comprises:

- (i) dissolving the crude Dutasteride in alcoholic solvents having C<sub>1</sub>-C<sub>5</sub> carbon atoms, preferably methanol;
- (ii) distilling the solvent from the reaction solution completely;
- (iii) scratching solid by using conventional methods to afford the novel amorphous form of Dutasteride.

The amorphous form of Dutasteride obtained I the above process is charecterized by X-ray powder diffraction pattern and Infrared spectrum.



The absorption frequencies of Infrared spectrum of novel amorphous form of Dutasteride which comprises 818.38,1041.03,1087.33,1132.58, 1177.86, 1219.18, 1242.20, 1263.01, 1318.98,1334.54,1364.57,1386.76,1434.50,1538.06,1592.95,1678.67,2875.18,2941.88, 3268.32 and 3468.27 cm<sup>-1</sup>.

Hence, the present invention is directed to provide novel amorphous form of Dutasteride and process for the preparation thereof. The process for the preparation of amorphous form of Dutasteride of the present invention is simple, eco-friendly and commercially viable.

The process of the present invention will be explained in more detail with reference to the following examples, which are provided by way of illustration only and should not be constructed as limit to the scope of the reaction in any manner.

**Example-1:**

**Process for the preparation of amorphous form of Dutasteride.**

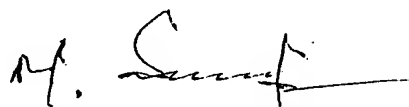
Dissolved 10 grams of crude Dutasteride (prepared as per the prior art methods) in 60 ml of methanol under stirring. Filter the reaction solution by washing with 20 ml of methanol. Distilled off the solvent completely under reduced pressure. Scratch the separated solid to get the desired amorphous form of Dutasteride (9.8 grams, 98% of yield).

## Claims

1. Novel amorphous form of  $17\beta$ -N-[2,5-bis (Trifluoromethyl) phenyl] carbamoyl-4-aza-5- $\alpha$ -androst-1-en-3-one (Dutasteride).
2. According to claim 1, the X-ray powder diffraction of novel amorphous for Dutasteride as depicted in figure-1.
3. The process for the preparation of novel amorphous form of Dutasteride which comprises ,
  - i) dissolving the crude Dutasteride in alcoholic solvents having  $C_1$ - $C_5$  carbon atoms, preferably methanol;
  - ii) distilling the solvent from the reaction solution completely;
  - iii) Scratching solid by using conventional methods to afford the novel amorphous form of Dutasteride.
4. Novel amorphous form of  $17\beta$ -N-[2,5-bis (Trifluoromethyl)phenyl]carbamoyl-4-aza-5- $\alpha$ -androst-1-en-3-one (Dutasteride), which is substantially as here in described and exemplified.

Dated: 23<sup>rd</sup> day of June 2003.

Signed)



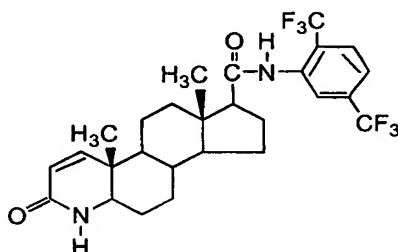
Dr. Manne Satyanarayana Reddy,  
Vice-President (R&D),  
Dr. Reddy's Laboratories Limited.

## ABSTRACT

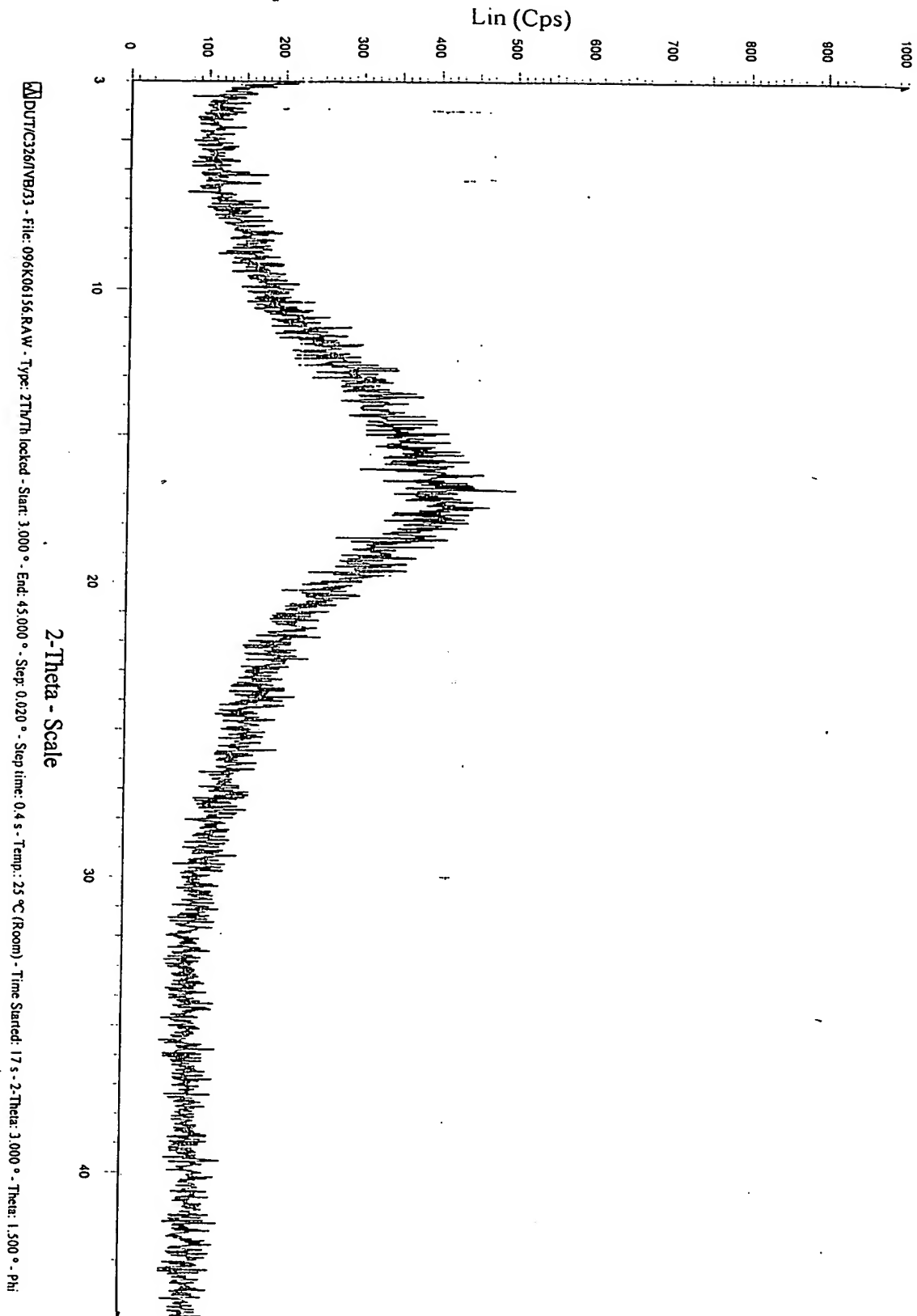
**Title of the invention:** "Novel Amorphous form of Dutasteride and Process for preparation thereof".

The present invention provides novel amorphous form of Dutasteride and process for preparation thereof. The amorphous of Dutasteride are characterized by X-ray diffractogram pattern. The process for the preparation of the amorphous form comprises the dissolution of Dutasteride in polar organic solvents accompanied by distillation of the solvent to afford the novel amorphous form.

Dutasteride can be depicted by the Formula (I).



Formula (I).



Dr. Manne Satyanarayana Reddy.

Dr. Reddy's Laboratories Limited.

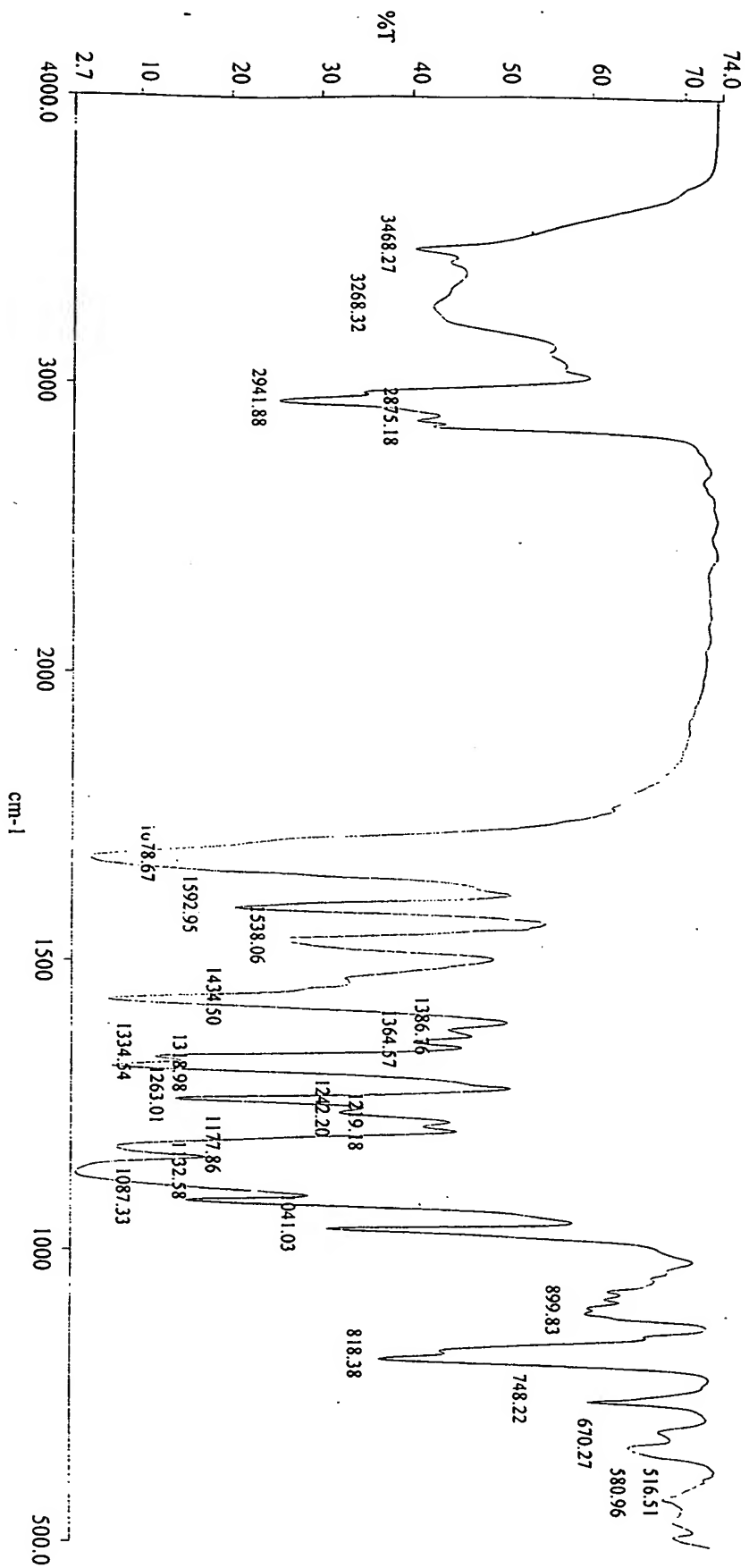


Figure 2 of 2.

Dr. Manne Satyanarayana Reddy.